HEM/ONC News

By Devon Schuyler

Apalutamide Approved for Use in Nonmetastatic Castration-Resistant Prostate Cancer

The US Food and Drug Administration (FDA) on February 14 approved the next-generation androgen receptor inhibitor apalutamide (Erleada, Janssen) to treat nonmetastatic castration-resistant prostate cancer. Apalutamide is the first approved treatment for this form of cancer.

Approval of apalutamide was based on the results of the phase 3 SPARTAN trial, which was published online by Smith and colleagues on February 8 in the *New England Journal of Medicine*. For the trial, the researchers randomly assigned in a 2:1 ratio 1207 men with nonmetastatic castration-resistant prostate cancer and a prostate-specific antigen doubling time of 10 months or less to receive either 240 mg of oral apalutamide or placebo each day. All patients continued to receive androgen deprivation therapy.

In a planned primary analysis, which was performed after 378 events had occurred, the median metastasis-free survival was 40.5 months in the apalutamide group vs 16.2 months in the placebo group (hazard ratio [HR] for metastasis or death, 0.28; 95% CI, 0.23-0.35; *P*<.001), a difference of more than 2 years. Apalutamide also was significantly more effective than placebo for the following secondary endpoints: median time to metastasis (40.5 vs 16.6 months), progression-free survival (PFS; 40.5 vs 14.7 months), and time to symptomatic progression.

The most common adverse reactions to apalutamide in the trial were fatigue, hypertension, rash, diarrhea, nausea, decreased weight, arthralgia, falls, hot flushes, decreased appetite, fractures, and peripheral edema. Apalutamide may also cause seizures.

Apalutamide, which was approved after receiving an FDA priority review designation, works by binding directly to the ligand-binding domain of the androgen receptor.

Durvalumab Approved for Unresectable Stage 3 NSCLC After Chemoradiation

The FDA on February 16 granted an expanded indication to durvalumab (Imfinzi, AstraZeneca) for the treatment of unresectable stage 3 non–small cell lung cancer (NSCLC) in patients without progression following concurrently administered platinum-based chemotherapy and radiation therapy. Durvalumab, an inhibitor of programmed death ligand 1 (PD-L1), was originally approved in 2017 to treat advanced urothelial carcinoma.

The expanded indication was based on a planned interim analysis of the PACIFIC trial, which was published by Antonia and colleagues in the November 16, 2017, issue of the *New England Journal of Medicine.* For the trial, a total of 713 patients with unresectable stage 3 NSCLC were randomly assigned in a 2:1 ratio to receive durvalumab at a dose of 10 mg/kg or a placebo every 2 weeks for up to 12 months. The study drug was infused within 42 days after the administration of platinum-based chemotherapy and radiation.

The median PFS from randomization was significantly longer with durvalumab than with placebo: 16.8 vs 5.6 months (stratified HR for disease progression or death, 0.52; 95% CI, 0.42-0.65; *P*<.001). In addition, the 12-month PFS rates were 55.9% vs 35.3%, and the 18-month PFS rates were 44.2% vs 27.0%. The objective response rate was higher with durvalumab than with placebo (28.4% vs 16.0%; *P*<.001), and the median duration of response was longer (72.8% of the patients given durvalumab vs 46.8% of the patients given placebo had an ongoing response at 18 months). Finally, the median time to death or distant metastasis was longer with durvalumab than with placebo (23.2 vs 14.6 months; *P*<.001).

Grade 3 or 4 adverse events occurred in 29.9% of patients in the durvalumab group and 26.1% of those in the placebo group; the most common grade 3 or 4 adverse event was pneumonia. Adverse events leading to drug discontinuation occurred in 15.4% of patients in the durvalumab group and 9.8% of those in the placebo group. The most common adverse reactions were cough, fatigue, pneumonitis/radiation pneumonitis, upper respiratory tract infections, dyspnea, and rash.

The recommended dosage of durvalumab for eligible patients with NSCLC is 10 mg/kg given as an intravenous infusion over 60 minutes every 2 weeks.

Durvalumab received priority review and breakthrough therapy designations from the FDA.

Also Approved

- On January 26, the FDA approved lutetium Lu 177 dotatate (Lutathera, Advanced Accelerator Applications USA), a radioactively labeled somatostatin analogue, for the treatment of somatostatin receptor–positive gastroenteropancreatic neuroendocrine tumors in adults.
- On March 20, the FDA approved brentuximab vedotin (Adcetris, Seattle Genetics) in combination with chemotherapy for adults with previously untreated stage III or IV classic Hodgkin lymphoma.